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Academic Detailing:

Physicians who provide medical services to Medicaid members should be aware that Heritage Information Systems, Inc. (Heritage) is working with the Kansas Medical Assistance Program (KMAP) to identify and address prescription drug utilization practices. The primary goal of this relationship is to identify and address opportunities to support high quality care rendered to Medicaid recipients while reducing overall program costs. Accomplishing this task involves a thorough analysis of prescription drug claims and medical data to identify those recipients who have opportunities for improving drug therapy outcomes and successes. Information about these patient cases will be provided to the prescribing physicians via mailings and site visits. The mailings will provide physicians with profile information pertaining to their patients and identify potential clinical opportunities for enhancing each patient's drug regimen. The profiles are useful for physicians in evaluating all medical-related services that have been rendered to each patient. In addition, a Kansas licensed pharmacist is traveling the state to meet with prescribers for the purpose of discussing specific clinical issues identified from drug regimen reviews. This activity, known as academic detailing, provides personal interaction between healthcare professionals and facilitates exchange of information, through the pharmacist, between physician prescribers and the Medicaid program.

We welcome the opportunity to discuss with you any comments or concerns you may have about this Newsletter. Please call our office at 1-800-745-1946 with any questions or concerns.

Kansas Medical Assistance Program
Drug Utilization Review Bulletin

Heritage Information Systems, Inc.

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Hyperlipidemia

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Coronary heart disease (CHD) is the single largest killer of American men and women. During 2001, CHD caused more than 1 of every 5 deaths. This year it is estimated that more than 700,000 Americans will have a new myocardial infarction (MI) and about 500,000 will have a recurrent attack. About 42 percent of the people who experience an MI will die from it, many from their first sign of CHD. Within 6 years after a recognized MI, 7 percent of men and 6 percent of women will experience sudden death. CHD imposes a major burden on society in terms of morbidity, mortality and economic costs. According to the 2004 Heart and Stroke Statistics, the total (direct and indirect) costs of care for CHD in 2004 is estimated to be $133 billion. Of the total direct costs, hospital and nursing home costs account for $43.7 billion and drugs/other medical durables for $8.5 billion.[1]

Elevated cholesterol is a known risk factor for CHD. Lowering cholesterol slows the progression of coronary artery lesions and decreases coronary event rates.[2] Recent clinical trials have demonstrated reductions in morbidity and mortality with LDL lowering therapy in particular with HMG-CoA reductase (statins) inhibitors.[3-7] Aggressive lowering of LDL cholesterol using statin therapy reduced the rates of fatal and nonfatal MI, stroke, revascularization procedures, and total mortality minimally by one quarter. Additionally, the Heart Protection Study demonstrated significantly reduced rates of MI, stroke and revascularization of about one quarter with statin therapy in high risk individuals irrespective of there baseline cholesterol levels.[8] In another recent study, ASCOT-LLA, statin therapy resulted in significant reductions in non-fatal MI and fatal CHD in hypertensive patients with at least 3 other risk factors and fasting total cholesterol levels less than 250 mg/dl. Other significant reductions occurred in secondary endpoints such as total cardiovascular events including revascularization procedures, total coronary events, and fatal and non-fatal stroke.[9]

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Results from Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 (PROVE-IT of the American College of Cardiology. This study enrolled 4,162 patients who were hospitalized for acute coronary syndromes within 30 days of study entry. Patients were randomized to 40 mg pravastatin (standard therapy) or 80 mg atorvastatin (intensive therapy). After treatment, the median LDL cholesterol level in the pravastatin group was 95 mg/dL compared to a median of 62 mg/dL (P <0.001) with intensive lipid-lowering therapy using atorvastatin. All-cause mortality was reduced by 28% in the aggressive-treatment arm, while death from MI was reduced by 18%. This study concluded that among patients who have recently had an acute coronary syndrome, an intensive lipid lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen.[10]

In 1985, the National Cholesterol Education Program (NCEP) was formed and the first cholesterol treatment guidelines were released in 1988. The most recent NCEP-Adult Treatment Panel (ATP) III guidelines were released in 2001.[2] All of the ATP reports emphasize LDL cholesterol as the primary target of therapy. A fasting lipid profiled is recommended on all adults 20 years of age and older and should be repeated every 5 years. If a nonfasting test is obtained, only the total cholesterol and HDL are usable. If total cholesterol is ≥ 200 mg/dl or HDL is < 40 mg/dl, then a follow-up fasting lipid panel is necessary to determine the treatment plan based on LDL. If a patient is hospitalized for acute coronary syndromes or coronary procedure, a lipid panel should be obtained on admission or within 24 hours.[2]

The presence or absence of CHD or CHD equivalents should be determined along with the presence of major risk factors to obtain the Framingham risk score. This risk assessment is the basis for determining the LDL goal and treatment plan. See tables 1, 2 and 3 for treatment guidelines.

Despite the information from recent trials and the NCEP guidelines, undertreatment is common. The Lipid Treatment Assessment Project (L-TAP) indicated that 63% of primary care physicians thought that cholesterol lowering has a great effect on reducing the risk of CHD and 36% thought is has a moderate effect. Additionally, 63% of the primary care physicians indicated that they follow the NCEP guidelines, "quite a bit," 31% stated they followed the guidelines "somewhat" and 2% did not follow the guidelines at all. Only 18% of the adults in this study with established CHD met the ATP II goal of less than 130 mg/dl.[11] In 2000, only 44% of Medicaid

> Approximately 72% of this population failed to reach an LDL cholesterol goal of less than 130 mg/dl.

patients hospitalized for heart attack, bypass surgery or angioplasty were screened for LDL cholesterol 60 and 365 days after discharge. Approximately 72% of this population failed to reach an LDL cholesterol goal of less than 130 mg/dl. In comparison, the Medicare and commercial rate of failure to reach the targeted LDL goal was 47%.[1] Considering the current LDL treatment goal of less than 100 mg/dl recommended in the NCEP ATP III guidelines, these rates are likely much worse than suggested.

The results of the L-TAP study suggested several reasons for suboptimal lipid management, including the use of inappropriately low drug doses, use of drugs with limited effectiveness, failure to select the appropriate drug for the type of lipid disorder and failure to consider tolerability of drug therapy and noncompliance.

Recently, underutilization of lipid lowering therapy was evaluated on the Kansas Medical Assistance Program population. The following table summarizes the results.

UNDERUSE: LIPID LOWERING (February 2003 through January 2004)	# Patients Identified
Discontinued Use: Antilipemic Therapy (primary prevention)	102
Discontinued Use: Antilipemic Therapy (secondary prevention)	645
Underutilization lipid lowering therapy [primary prevention]	2087
Underutilization of lipid lowering therapy [2nd prevention]	6665
Total	**9499**

Patients with a history of CHD or CHD risk equivalents as determined by diagnoses, procedures or drug use, or with risk factors placing them at moderate to high risk for developing CHD were considered candidates for lipid lowering therapy. Patients with a history of hepatic impairment were not considered candidates for lipid lowering therapy.

Statins are the most effective LDL lowering agents and are the drug of choice for lowering LDL levels. LDL reductions are dose dependent and differ among the statins ranging from 31 percent to 63 percent. Statins also effectively decrease triglyceride levels. They have modest effects on raising HDL levels ranging from 2 percent to 16 percent.. Statin mono-therapy is generally well tolerated by most persons and is associated with few adverse effects.[12] The most serious side effects are hepatic and skeletal muscle toxicity. Elevated transaminase levels occur in about 0.5 to 2% of cases and are dose dependent. Progression to liver failure is rare. Reversal of transaminase elevation occurs with dose reductions and often do not recur with re-challenge or use of another statin. Liver function tests should be performed at initiation of treatment and before dosage increases. Myopathy is less common than increases in liver enzymes and is estimated to occur in approximately 0.1% of patients who receive statin monotherapy. In rare cases, myopathy has progressed to rhabdomyolysis and acute renal failure. Rhabdomyolysis related deaths have been reported with all statins except for fluvastatin.[12,13] The use of statin therapy in combination with fibrates carries a greater risk of myopathy than when statins are used alone. However, moderate statin doses with fibrates in individuals without multiple comorbidities or multiple medications appears to carry a relatively low incidence of myopathy. Safety considerations for statin associated myopathy have been outlined in the ACC/AHA/NHLBI advisory on statins.[12] Some of the risk factors outlined include advanced age, small body frame, multiple comorbidities (e,g, renal insufficiency especially due to diabetes), multiple medications, perioperative periods, drug interactions (fibrates, niacin [rare occurrence], cyclosporine, azole-antifungals, macrolide antibiotics, protease inhibitors, verapamil, amiodarone, alcohol abuse and consumption of greater than one quart of grapefruit juice per day).[12] Table 4 summarizes the effect of statins along with other available antilipemic drugs and classes.

...moderate statin doses with fibrates in individuals without multiple comorbidities or multiple medications appears to carry a relatively low incidence of myopathy.

Table 1. Risk Factor Assessment for CHD[2]

Positive Risk Factors	Negative Risk Factors
Male ≥ 45 years Female ≥ 55 years or premature menopause without estrogen replacement therapy	HDL-cholesterol > 60 mg/dL
Family history of CHD (Sudden death or definite MI of parent or other first degree relative): • Males <55 years old • Females <65 years old	
Current smoker	
Hypertension (BP≥ 140/90 mmHg, or taking antihypertensive medication)	
HDL-cholesterol <40 mg/dL	

^Add all positive risk factors and subtract any negative risk factor. For example, if the patient is male > 45 years old, has hypertension and an HDL cholesterol > 60mg/dL, he would have a total of 1 risk factor

Table 2. LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories[2]

Risk Category	LDL goal (mg/dL)	LDL level at which to initiate TLC (mg/dL)	LDL level at which to consider drug therapy (mg/dL)
CHD or CHD Risk Equivalents** (10-year risk > 20%)	< 100	≥ 100	≥ 130 (100-129: drug therapy optional)
2+ Risk Factors (10-year risk ≤ 20%)	< 130	≥ 130	10-year risk 10-20%: ≥ 130 10-year risk < 10%: ≥ 160
0 - 1 Risk Factor	< 160	≥ 160	≥ 190 (160-189: drug therapy optional)

*CHD risk equivalents include peripheral artery disease, abdominal aortic aneurysm and symptomatic carotid artery disease, diabetes, an ATP III Framingham based CHD 10-year risk assessment greater than > 20%). Diabetes qualifies as a CHD risk equivalent because it confers a high risk of new CHD within 10 years.

Table 3. Therapeutic Lifestyle Changes (TLC) Diet Recommendations[2]

Nutrient	**Recommended Intake**
Saturated Fat	<7% of total calories
Polyunsaturated Fat	Up to 10% of total calories
Monounsaturated Fat	Up to 20% of total calories
Total Fat	25-35% of total calories
Carbohydrates	50-60% of total calories
Fiber	20-30 g/d
Protein	Approximately 15% of total calories
Cholesterol	< 200 mg/d
Total Calories	Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain

- If the patient is a young man or premenopausal woman with moderately high LDL cholesterol (160 – 189 mg/dL), lipid lowering should be accomplished through physical activity and diet unless the patient has multiple risk factors, particularly smoking or a family history of CHD.
- When to initiate the TLC Diet depends on the individual patient and their corresponding LDL goal level as noted in Table 2.

Table 4. Effects of Antilipemics on Lipids[14-21]

Treatment	↓LDL Level (%)	↑HDL Level (%)	↓TG Level (%)	↓TC Level (%)
Atorvastatin (Lipitor®)10, 20, 40, 80 mg q.d.	39-60	5-9	19-37	29-45
Fluvastatin (Lescol®) 20, 40, 80 mg q.d.	22-36	3-7	12-19	17-27
Lovastatin (Mevacor®) 10, 20, 40 mg q.d.	24-40	2-8	6-10	16-24
Pravastatin (Pravachol®) 10, 20, 40 mg q.d.	22-34	7-12	11-24	16-25
Rosuvastatin (Crestor®) 5, 10, 20, 40 mg qd	45-63	8-14	10-35	33-46
Simvastatin (Zocor®) 5, 10, 20, 40, 80 mg q.d.	26-47	8-16	12-33	19-36
Gemfibrozil (Lopid®) 600 mg b.i.d.	1-10	6-10	31-43	4-11
Fenofibrate (Tricor®, Lofibra®) 200 mg q.d.	21	11	29	19
Nicotinic acid 500 mg-2 g q.d.	5-25	15-35	20-50	2-12
Bile acid sequestrants'	15-30	3-5	0-20	4-10
Ezetimibe (Zetia®) 10 mg q.d.	18-19	4-5	8	13
Niacin 500 mg-2 g q.d./lovastatin 10-40 mg q.d. (Advicor®)	30-42	20-30	32-44	24-33
Fibrate + statin	26-36	19-22	41-53	21-36
Ezetimibe (Zetia) + statin	21-50	3-9	11-24	17-37

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